## REMARKS

Applicants would like to thank the Examiner for withdrawal of the previous rejections.

The formulation of a biologically active agent with a biodegradable polymer can provide for sustained release of the agent into a patient. However, most of these formulations must be surgically implanted, or can be injected only through a needle having a large diameter. The formulation of biologically active agents with various liquids can provide for the administration of the agent through a needle of standard size, for example a 23-gauge needle or smaller. This can greatly improve patient compliance to the therapy. However, such formulations typically do not provide acceptable control over the rate with which the biologically active agent is released into the patient. The present invention overcomes these problems.

The claimed invention includes an injectable formulation, including hyaluronic acid dissolved in a physiological buffer, and particles, the particles including a biologically active agent and a biocompatible polymeric matrix. This formulation provides for the administration of a biologically active agent into a patient.

*Rejection of claims under 35 U.S.C. § 112, first paragraph (enablement)*

Rejection of claims 21-31, 33 and 34 under Section 112, first paragraph for failing to satisfy the enablement requirement is respectfully traversed.

The instant specification provides a sufficient description of about how to make and use the invention as claimed. In particular, the Examples describe 11 different microsphere formulations wherein the polymeric matrix was altered according to the following variables: polymer molecular weight (8kD, 10kD, and 31kD), polymer end group (capped or uncapped) and the amount of zinc carbonate added as an excipient (0%, 1%, 3%, and 6%). See Specification at pages 17-18. Furthermore, the specification teaches that these assorted formations may be prepared in the presence of at least five different biologically active agents. See Specification at pages 17-21 and 24-25. By disclosing at least 55 different examples, use with needles of a variety of gauges (including 23 gauge and smaller), and supporting data, the written description adequately provides teaching and guidance on how to make and use the

claimed invention. The disclosed formulations are readily applicable and fully enabled for all types of biologically active agents.

A specification disclosure is presumed to be in compliance with the enablement requirement, unless there is some reason to doubt the objective truth of the statements contained therein that must be relied on for enabling support. The Office bears the burden of explaining why it doubts the truth or accuracy of any statement in a supporting disclosure and this burden is only met where the examiner makes specific findings of fact, supported by evidence, as a basis to justify its explanation. MPEP 2164.04, citing *In re Marzocchi*, 439 F.2d 220, 224 (C.C.P.A. 1971).

The Office has rejected the claims under Section 112, first paragraph for lack of enablement. The Office's apparent justification for this rejection is the belief that the specification "only discloses cursory conclusions (pages 3-4 [referring to the SUMMARY SECTION]) without data supporting the findings..." The Office has merely stated that the description is not adequate without pointing out what is missing that otherwise must be present in order to render the claimed invention fully enabled. The Office has not met its burden to sustain this rejection under Section 112, first paragraph for lack of enablement; therefore, Applicants respectfully request that this rejection be withdrawn.

*Rejection of claims under 35 U.S.C. § 112, second paragraph (definiteness)*

The rejection of claims 20, 30, and 31 under 35 U.S.C. § 112, second paragraph, has been obviated in part by appropriate amendment.

The rejection of claims 21-23, 25-31, 33, 34, and 36 under 35 U.S.C. § 112, second paragraph, as being indefinite as to whether hyaluronic acid is part of a "biologically active agent", is respectfully traversed.

Indefiniteness does not arise merely because an element of a claim is subject to multiple inclusion. MPEP 2173.05(o). Claim element (a) specifies "hyaluronic acid dissolved in a physiological buffer." This language means that, regardless of what is in the particles, hyaluronic acid is present in the physiological buffer of the injectable formulation. Claim

element (b) specifies "particles, comprising (i) a biologically active agent, and (ii) a biocompatible polymeric matrix." This language means that, regardless of the composition of the physiological buffer, the particles contain a biologically active agent and a biocompatible polymeric matrix in the injectable formulation. Accordingly, hyaluronic acid is present in the physiological buffer, no matter what biologically active agent is used. Furthermore, the claims do not exclude hyaluronic acid from the particles.

Applicants submit that the metes and bounds of the claims are clear and definite. Applicants respectfully request that the rejection of these claims be withdrawn.

*Rejection of claims under 35 U.S.C. § 102 and § 103(a)*

The rejection of claims 17, 21, 23, 25-29, 34 and 35 under 35 U.S.C. § 102 and § 103(a) over Cleland *et al.* (U.S. Patent No. 6,113,947, filed June 17, 1997), alone or in combination with page T515 of the Aldrich Catalog (1996-1997) is respectfully traversed. Cleland *et al.* is not anticipatory because it discloses hyaluronic acid as only one of literally millions of compounds suitable for formulations. Furthermore, the unexpected and surprising properties of hyaluronic acid, which allow injection in much smaller needles, demonstrate the unobviousness of the claimed invention.

Cleland *et al.* teach the use of hyaluronic acid as a dispersant in a viscous physiologically acceptable solution. Among the dispersants listed, this reference cites: surfactants, polysaccharides (with hyaluronic acid included as an example), protamine sulfate, polyethylene glycol 400, among others (col. 19, ll. 48-58). Given the breadth of this list, the reference can be considered to anticipate the present invention. Accordingly, the claimed invention is not anticipated by these references. Furthermore, the unexpected and surprising properties of hyaluronic acid, which allow injection in much smaller needles, shown in examples in the present application, demonstrate the unobviousness of the claimed invention. Applicants respectfully request that this rejection be withdrawn.

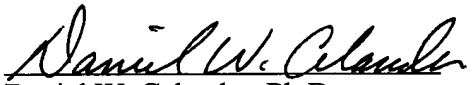
The rejection of claims 17, 21, 25-29 and 35 under 35 U.S.C. § 102 over McGinity *et al.* (U.S. Patent No. 5,288,502, Feb. 22, 1994) is respectfully traversed. McGinity *et al.* do not describe inclusion of hyaluronic acid dissolved in a physiological buffer.

McGinity *et al.* teach the use of hyaluronic acid as a stabilizing agent for multiphase polymeric microspheres (col. 27, l. 61 to col. 28, l. 17). Among the stabilizing agents listed, this reference cites: sugars, polysaccharides, amino acids, peptides, mucopolysaccharides (with hyaluronic acid included as an example), pluronic, polyethyleneglycols, polyacrylates, PVP, and PVA. (col. 28, ll. 4-17). There is no description nor suggestion that hyaluronic acid be included in a physiological buffer of an injectable formulation. There is no suggestion that inclusion of hyaluronic acid will allow for injection in smaller needles. Applicants respectfully request that this rejection be withdrawn.

Claims 37 stands objected as being dependent upon a rejected base claim. In light of Applicants' remarks to the Examiner's rejection of the claims, Applicants request that the objection to claims 37 be withdrawn.

Applicants submit that the present application is in condition for allowance. Early notice of such action is earnestly solicited.

Respectfully submitted,



Daniel W. Celander, Ph.D.
Registration No. 52,710
Representative for Applicant

SONNENSCHEIN NATH & ROSENTHAL
P. O. BOX 061080
WACKER DRIVE STATION, SEARS TOWER
CHICAGO, IL 60606
(312) 876-8071